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ORIGINAL ARTICLE

Therapeutic effects of transurethral incision of the bladder neck on primary bladder neck dysfunction refractory to alpha-adrenergic blockade in men

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Summary *Background:* Dysfunctional voiding is an abnormality of bladder emptying in neurologically normal individuals where the external sphincter activity increases during voiding, and it is difficult to diagnose by symptoms alone. Videourodynamic study could provide great help in differentiating dysfunctional voiding and other voiding disorder. In this retrospective study, we analyze the videourodynamic parameters of the patients with dysfunctional voiding.
Purpose: To investigate the clinical presentations and videourodynamic characteristics of adult women with dysfunctional voiding (DV).
Methods: A total of 1605 women with lower urinary tract symptoms (LUTS) were investigated with videourodynamic (VUD) studies from 1997 to 2010. The clinical urinary symptoms and VUD characteristics of DV were compared with a group of urodynamically normal controls. Antimuscarinic or alpha-blocker treatment, with or without a skeletal muscle relaxant according to the chief complaint was given.
Results: There were 168 women diagnosed with DV. Detrusor overactivity (DO) occurred in 69% of women with DV. Patients with DV had significantly lower cystometric bladder capacity, higher detrusor pressure, lower maximum flow rate, and larger post-void residual volume than the controls. A total of 114 (67.9%) patients had storage symptoms and 54 (32.1%) had voiding symptoms as their chief complaints among those with DV. Among them, urinary frequency ($n = 69$, 41.1%) was the most common chief complaint, followed by dysuria ($n = 54$, 32.1%), and urgency incontinence ($n = 26$, 15.5%). The incidence of urgency incontinence and dysuria were significantly greater than that in the control group, however, the incidence

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of frequency, urgency, or nocturia showed no significant difference between DV and control groups. Recurrent UTI was a common adverse event, and happened in 20 patients (12%) with DV. The medication, alpha-blocker or antimuscarinic agent, was prescribed to the patients with DV according to their symptoms. The success rates were 41.2% ($n = 47$) for antimuscarinic therapy and 51.9% ($n = 28$) for alpha-blocker therapy in patients with storage and voiding LUTS, respectively ($p = 0.366$).

Conclusion: DO and storage LUTS commonly occurred in women with DV, suggesting DO could be one of the etiology in the pathophysiology of DV. VUD studies yielded a high diagnostic rate for DV in women with LUTS.

1. Introduction

Primary bladder neck dysfunction (BND) is considered an important cause of chronic voiding dysfunction in young and middle-aged men and women. Wang et al reported that 41% of young men with lower urinary tract symptoms (LUTS) and low uroflow experienced primary BND.[1] BND is also noted in women with LUTS, and the prevalence rate has been reported to be between 1 and 16%.[2,3] Medical treatment with alpha-blockers or transurethral incision of the bladder neck (TUI-BN) is considered the standard treatment for primary BND.[4] However, the diagnosis of BND should be carefully made by means of the video-urodynamic study (VUDS).[2]

Previous studies revealed that peak voiding pressure decreased and voiding function improved in patients with classical BND after TUI-BN.[4,5] Although a high voiding pressure and a narrow bladder neck in voiding cystourethrography are considered essential diagnostic criteria for BND, we have observed patients with voiding dysfunction having low or normal voiding pressures and narrow bladder necks during VUDS. Recently, Ke and Kuo found that detrusor contractility was restored after TUI-BN for treatment of BND in patients with high-level spinal cord injuries and detrusor underactivty.[6] Interruption of the alpha-adrenergic afferent nerves that inhibit detrusor contractility has been postulated for this therapeutic result after TUI-BN. It was the purpose of this study to investigate whether similar recovery of detrusor contractility also occurs in neurologically intact men with BND after TUI-BN.

2. Materials and methods

We retrospectively evaluated the surgical outcomes of male patients diagnosed to have BND who underwent TUI-BN from 1999 to 2009. A total of 46 patients fulfilled the diagnostic criteria for BND and had repeated VUDS after TUI-BN. All patients were first treated with alpha-blockers; TUI-BN was performed after failure of the medical treatment for at least 6 months. The medical treatment failure was defined as persistent LUTS without improvement under the continuous alpha adrenergic blocker therapy for at least 6 months reported by patients themselves and bladder neck narrowing at the time of voiding confirmed by VUDS. Patients with a history of pelvic trauma, diabetes mellitus, congenital urogenital diseases, neurologic disorders, previous lower urinary tract surgery, and urinary tract malignancy were excluded from the study.

VUDS was performed according to the recommendations of the International Continence Society.[7] VUDS was performed using a 6-Fr dual lumen transurethral catheter, with infusion of 20% urographin at a rate of 20—30 mL/min. Abdominal pressure was recorded using an 8-Fr pediatric nasogastric tube mounted with a balloon inflated with 5 mL of normal saline. Urethral sphincter electromyography was performed using surface patch electromyography electrodes placed at the perianal area. VUDS was performed in the standing position and fluoroscopy of the urinary bladder and urethra was performed using a C-arm fluoroscope in the posteroanterior position, projecting from the buttocks so that the bladder neck and urethra could be demonstrated properly. The urodynamic parameters of the maximum flow rate (Qmax), post-voiding residual (PVR) volume, voided volume, and voiding detrusor pressure at Qmax (PdetQmax) were recorded in detail. Unopened or inadequate funneling of the bladder neck during the voiding phase, together with low Qmax, was considered indicative of BND (Fig. 1A).[6] In addition, the total prostate volume was measured by transrectal sonography of the prostate (B-K Medical ultrasound with 8818 transducer, Peabody, MA, USA), which was performed by an experienced urologist. The volume was calculated as TPV (mL) = length × width × height × 0.52. The volume of the transition zone of prostate was calculated by the same method and the transition zone index was defined as the transition zone volume divided by the total prostate volume.

TUI-BN was performed with an adult resectoscope and diathermy electrode using a power setting of 120 W. Double incisions were made at the 5 and 7 o'clock positions of the bladder neck, with an attempt to view the serosal layer. The external urethral sphincter and the prostate were not targeted. Patients were catheterized with an indwelling Foley catheter after the procedure, and a voiding trial was started 48 hours after surgery.

This study was approved by the Institutional Review Board of the hospital. Informed consent was obtained from all patients before performing any operation and patients were informed of the possible procedural complications, such as postoperative bleeding, retrograde ejaculation, and urinary incontinence.

The therapeutic outcome was graded on the basis of changes in a validated 6-scale patient perception of bladder condition (PPBC) questionnaire.[8] Mild improvement was

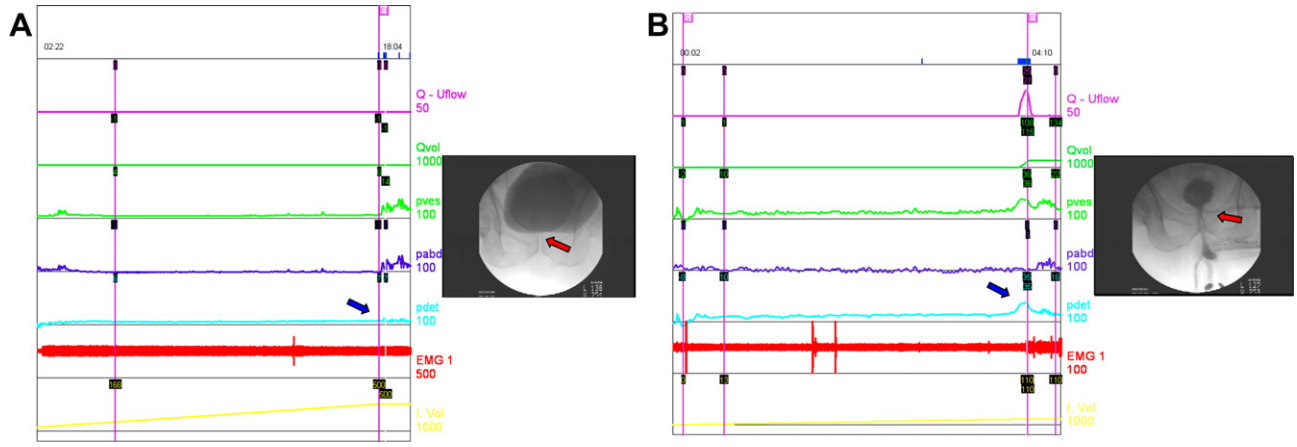

Figure 1 Video-urodynamic studies (VUDS) at baseline (A) and after transurethral incision of the bladder neck (TUI-BN) in one patient with bladder neck dysfunction and low voiding pressure (B). The bladder neck was wide open and the voiding pressure and maximum flow rate were increased after TUI-BN. (A) VUDS at baseline. The detrusor muscle was non-contractile (blue arrow) and the bladder neck did not open during the voiding phase on cinefluoroscopy (red arrow). (B) VUDS after TUI-BN. The patient regained detrusor contractility (blue arrow) and the bladder neck opened widely during the voiding phase on cinefluoroscopy (red arrow).

defined as improvement by 1 point, moderate improvement, by 2 points and marked improvement, by 3 points. Patients with moderate or marked improvement were considered to have experienced successful results.

According to changes in PdetQmax between the baseline values and those after TUI-BN, the patients were categorized into three groups: increased-Pdet, decreased-Pdet, and no change groups. A change of 10 or more cm H_2O in PdetQmax between baseline and postoperative values was considered significant. Qmax, voided volume, PVR volume, and PdetQmax were compared between baseline and after TUI-BN, and among the three groups. Patients completed the PPBC, and a score indicative of treatment success on the PPBC was regarded as the primary end-point of the treatment.

The Wilcoxon test was performed by using SPSS software for Windows (Version 10.0, SPSS, Chicago, Illinois, USA). A p value of <0.05 was considered statistically significant.

3. Results

The mean age of the 46 patients at diagnosis was 60.6 $\pm$ 12.8 years (range = 22—83 years). The follow-up period was 3.0 $\pm$ 2.7 years (range = 1—12 years). The mean total prostate volume was 26.5 $\pm$ 9.3 mL (range = 11.3—47.9 mL) and the mean transition zone index was 0.29 $\pm$ 0.09 (range = 0.17—0.54).

As compared to baseline values, PdetQmax decreased in 28 patients, increased in 12, and had no change in the other 6 after TUI-BN. Overall, the mean Qmax increased (baseline vs post-TUI-BN, 5.72 $\pm$ 4.77 vs 13.7 $\pm$ 8.02 mL/second, $p < 0.001$), the voided volume increased (146 $\pm$ 130 vs 185 $\pm$ 109 mL, $p = 0.03$) and PVR decreased (214 $\pm$ 200 vs 108 $\pm$ 136 mL, $p < 0.001$) significantly after TUI-BN. The bladder neck became wide open and had a funnel shape during voiding in all patients after TUI-BN (Fig. 1B).

Table 1 shows that the mean Qmax increased, the voided volume increased, and the PVR volume decreased significantly after TUI-BN in both the increased-Pdet and decreased-Pdet groups. PdetQmax significantly increased and decreased in the increased Pdet and decreased Pdet group after TUI-BN, respectively. The other six patients maintained low detrusor contractility and large PVR volumes after TUI-BN. Among the patients with no change in detrusor contractility after TUI-BN, four voided efficiently, with assistance of abdominal pressure, while the remaining two patients had persistent voiding difficulty. No major complications, such as bleeding, urinary incontinence, or retrograde ejaculation, were reported. PPBC improved by 2 scales after TUI-BN in 36 (78%) patients, including 22 (79%) in the decreased-Pdet group, 10 (83%) in the increased-Pdet group, and 4 (67%) with persistent detrusor underactivity.

4. Discussion

This study showed that TUI-BN improved voiding function in most patients with primary BND, with or without high voiding pressure before surgery. Patients with BND are usually treated with alpha-blockers, and when medical therapy fails to improve urinary symptoms, surgery with TUI-BN seems to be effective,[5,9,10] which was concretely confirmed by the results of this study. Improved bladder voiding function was achieved by TUI-BN in patients with BND and impaired detrusor contractility. Even in the patients with persistent detrusor underactivity, 67% of them voided adequately with the aid of abdominal straining.

In the past, no BND pathophysiology was definitively elucidated, but several theories were postulated. The initial theory focused on the structural change of the bladder neck, e.g., fibrosis or hyperplasia.[1] Smooth muscle hypertrophy, fibrous changes and inflammatory changes were also reported as the possible causes of BND.[11] Some studies suggested that BND could be caused by abnormalities of the striated urethral sphincter muscle, and this

Table 1 Changes of urodynamic parameters in patients with BND before and after TUI-BN.

	Pre-TUI-BN	Post-TUI-BN	*p*
Increased-Pdet ($n = 12$)			
PdetQmax (cmH_2O)	8.7 ± 9.8	28.3 ± 13.8	0.006
Qmax (mL/s)	3.9 ± 4.5	13.3 ± 5.3	0.002
Voided volume (mL)	89.1 ± 138	202 ± 101	0.05
PVR (mL)	307 ± 182	131 ± 141	0.03
Voiding efficiency (%)	22.5% ± 43.1%	60.7% ± 41.7%	0.038
Decreased-Pdet ($n = 28$)			
PdetQmax (cmH_2O)	65.2 ± 47.1	40.1 ± 32.6	0.012
Qmax (mL/s)	3.9 ± 4.5	10.0 ± 9.4	0.04
Voided volume (mL)	110 ± 135	140 ± 121	0.14
PVR (mL)	328 ± 297	175 ± 171	0.08
Voiding efficiency (%)	25.1% ± 31.3%	44.4% ± 41.4%	0.054
No change-Pdet ($n = 6$)			
PdetQmax (cmH_2O)	0.3 ± 0.8	0.3 ± 0.8	1.00
Qmax (mL/s)	3.4 ± 5.8	5.7 ± 8.8	0.571
Voided volume (mL)	50.6 ± 88.0	87.1 ± 117	0.522
PVR (mL)	397 ± 261	310 ± 188	0.491
Voiding efficiency (%)	11.3% ± 25.2%	21.9% ± 38.4%	0.584

dysfunctional external sphincter extended to the bladder neck in 48% of men.[12–14] Recently, the concept of sympathetic inhibition was raised and neuropeptide Y was considered as a possible neurotransmitter for bladder neck dyssynergia.[12,15–19] In addition to sympathetic hyperactivity, decreased acetylcholine release over time was also considered as a possible cause influencing bladder contractility. Decreased acetylcholine levels in rat bladders were also found in association with partial bladder outlet obstruction.[20] These experimental results help explain why low detrusor contractility is present in patients with primary BND.

In clinical practice, the key diagnostic criterion of BND is the characteristic appearance of a narrowed or unopened bladder neck, while elevated voiding pressure is usually, but not always, present in these cases.[21,22] In our study, 12 patients with low Pdet at baseline had improved bladder voiding function after TUI-BN. This finding is quite different from previous observations, that patients with BND should have a high voiding pressure, and the decreased voiding pressure and increased urinary flow rate are always noted after TUI-BN.[4,5]

During normal voiding, detrusor contraction starts following urethral sphincter relaxation and bladder neck funneling. The bladder neck and external urethral sphincter are innervated by the sympathetic nervous system.[12,13] The role of sympathetic nerves on bladder filling has recently been emphasized. Alpha-adrenergic nerves are postulated to inhibit reflex activation of the detrusor muscle during bladder filling, while beta-adrenergic nerves relax the detrusor muscle.[23] Experimental data support that the released norepinephrine exerts an inhibitory effect on detrusor function by adrenergic innervation.[24]

In patients with BND and low detrusor voiding pressure, detrusor contractility could be inhibited by a poorly relaxed bladder neck, due to sympathetic hyperactivity. We observed increased detrusor pressure after TUI-BN in high-level spinal cord injury patients with low voiding pressure at baseline. Increased sympathetic tone was speculated as a possible cause to inhibit the detrusor contractility in these neuropathic patients.[6] TUI-BN might disrupt the afferent limb of sympathetic innervation, reduce sympathetic hyperactivity of the bladder neck, and decrease the inhibitory effect on the detrusor nucleus, and finally, detrusor contractility probably recovered after TUI-BN surgery.

TUI-BN is a safe procedure for treating BND, although some minor complications have been reported. In 2006, Navalon et al reported that retrograde ejaculation after TUI-BN was a concern, especially when operating on young men.[10] Yang et al reported that preserving a portion of the supramontanal prostatic tissue during TUI-BN preserved the function of antegrade ejaculation.[25] Urinary incontinence is found in 8.3% of women after TUI-BN, and inadvertent injury to the urethral sphincter is likely to be responsible for this complication.[26] In this study, we performed TUI-BN only targeting the bladder neck, without extension of the incision to the urethral sphincter, and probably on this account, no such adverse event was reported among our patients.

An accurate diagnosis of BND is important because medical treatment failure can be successfully treated by TUI-BN. Turner-Warwick advocated the use of urodynamic studies and voiding cystourethrography to diagnose BND in men aged $\leq$50 years with long histories of LUTS.[27] Patients with BND may present with low urinary flow rate and non-specific findings on cystoscopy, such as small prostates, tight bladder necks, and trabeculated bladder walls. VUDS provides data for a more accurate diagnosis of BND.[1,4,5] Bladder neck incision without prior urodynamic evaluation is useless in managing neurogenic bladder dysfunction.[28]

Male LUTS can result from a complex interplay of pathophysiologic features which include bladder dysfunction

and bladder outlet dysfunction such as benign prostatic obstruction, BND, or poor relaxation of the urethral sphincter.[29] VUDS is routinely performed in our department for differential diagnosis of male LUTS refractory to initial medical therapy. Although VUDS is an accurate diagnostic tool to find patients with BND by high voiding detrusor pressure and narrow bladder necks, it is difficult to diagnose patients with BND combined with detrusor underactivity. In this study, low voiding pressure and large PVR persisted after TUI-BN in six patients. In these patients with detrusor underactivity, the detrusor function could take a longer time to recover, or the main cause for their voiding dysfunction was detrusor failure. However, some of these patients voided more efficiently with the aid of abdominal straining because TUI-BN decreased the resistance of the bladder neck.

The limitations of this study were its small sample size and retrospective design. A control arm is also lacking, because patients with voiding dysfunction could recover spontaneously without surgical intervention. Further investigation of the histopathology of the bladder neck between groups with different detrusor pressure changes after TUI-BN would help reveal the possible mechanisms of BND.

5. Conclusion

TUI-BN is an effective treatment for primary BND diagnosed by VUDS, in view of the fact that most patients with BND and low voiding pressures or underactive detrusor muscles, as well as those with high voiding pressures, benefited from TUI-BN.

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